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Chronic Atrial Fibrillation

Success of Serial Cardioversion Therapy and Safety of Oral Anticoagulation

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Background: Serial electrical cardioversion is often used for treatment of atrial fibrillation, but its long-term efficacy has not been determined prospectively.

Objectives: To determine the long-term success rate of the serial electrical cardioversion approach in patients with chronic atrial fibrillation, to identify factors that predict its success, and to assess the efficacy and safety of oral anticoagulation in these patients.

Methods: Patients with chronic (>24 hours) atrial fibrillation received anticoagulant therapy for at least 4 weeks prior to electrical cardioversion. No prophylactic antiarrhythmic agent was given after the first shock. Relapses were managed by using repeated cardioversions, after which serial antiarrhythmic drug therapy was started. Treatment with anticoagulants was withdrawn after 4 weeks of sinus rhythm.

Results: Two hundred thirty-six patients were followed up for a mean \pm SD of 3.7 ± 1.6 years. The actuarial cumulative percentages of patients who main-

tained sinus rhythm after serial cardioversion treatment was 42% and 27% after 1 and 4 years, respectively. Multivariate analysis showed that factors that were associated with failure of this approach included duration of atrial fibrillation that exceeded 36 months (risk ratio, 5.0; $P < .001$), poor exercise tolerance (functional class III; risk ratio, 1.8; $P = .001$), and age older than 56 years (risk ratio, 1.5; $P = .04$). The anticoagulation level (international normalized ratio, 2.4-4.8) was associated with an incidence of thromboembolic events and bleeding complications of 0.2% and 1.5%, respectively.

Conclusions: Many patients with chronic atrial fibrillation failed to respond to the serial electrical cardioversion strategy. However, in younger patients with a fair exercise tolerance and a duration of atrial fibrillation shorter than 36 months, this approach may be worthwhile. In addition, thromboembolic events were infrequent in the patients who were subjected to this regimen.

Arch Intern Med. 1996;156:2585-2592

THE DC ELECTRICAL cardioversion is an effective and safe method to obtain sinus rhythm in patients with chronic atrial fibrillation, but the procedure is not always successful.^{1,2} To prevent a recurrence of atrial fibrillation, antiarrhythmic drug therapy is often prescribed. Despite this, frequent relapses of atrial fibrillation occur,³⁻¹⁰ and occasionally drug treatment is associated with adverse events.^{11,12} However, patients may remain at risk for a thromboembolic event after recurrence of the arrhythmia, while they are already no longer receiving warfarin sodium. Up until now, there have been only limited data on the long-term outcome of serial electrical cardioversion therapy.^{13,14} Moreover, previous studies usually did not evaluate patients who did not respond to electrical cardioversion, and this might have caused selection bias.

These drawbacks preclude a reliable assessment of the patient characteristics that determine the long-term prognosis for atrial fibrillation. Thus, the notion that arrhythmia outcome is favorable in about half of the patients may be erroneous.

The aim of the present prospective study was 2-fold: (1) to investigate the long-term outcome of a serial electrical cardioversion approach combined with serial prophylactic antiarrhythmic drug therapy and determine the factors that predict its success and (2) to assess the efficacy and safety of oral anticoagulation therapy in patients with chronic atrial fibrillation by using this strategy.

*See Patients and Methods
on next page*

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PATIENTS AND METHODS

In the course of 7 years (January 1986–January 1993), 426 consecutive patients with chronic atrial fibrillation were referred to our hospital for treatment. Criteria for chronicity of atrial fibrillation were at least 2 electrocardiographic documentations and continuous presence on a 24-hour Holter recording. Neither patient age nor duration of atrial fibrillation was an exclusion criterion for participation in the study. Exclusion criteria were New York Heart Association class IV for exercise tolerance ($n=60$), unstable angina pectoris ($n=10$), or acute myocardial infarction less than 4 weeks earlier ($n=14$). Patients were also not included in this series if they had a relapse of chronic atrial fibrillation while they were receiving an antiarrhythmic drug prior to the inclusion into the present study ($n=106$). The remaining 236 patients were subject to evaluation; some of them have been described previously.^{2,7,14} The study was approved by the local institutional review board, and written informed consent was given by all patients.

Electrical cardioversion was the principal treatment of atrial fibrillation. After the first cardioversion, no antiarrhythmic drug therapy was started. In contrast, following a relapse of the arrhythmia, our serial prophylactic antiarrhythmic drug strategy was applied. In the case of failure to reestablish sinus rhythm, the rate control alternative was adopted (**Figure 1**). Each electrical cardioversion was performed on an elective basis. The protocol has been described before.² In short, patients received warfarin or a derivative at least 4 weeks prior to the procedure. The target prothrombin time was an international normalized ratio of 2.4 to 4.8. Efficacy of anticoagulation was monitored by a regional thrombosis center. Such services are specialized in the monitoring of coumarin therapy for outpatients. On

the day of electrical cardioversion, a 2-dimensional trans-thoracic echocardiographic assay was done. During this procedure, left and right atrial dimensions, as well as left ventricular dimensions, were determined according to the method of Schiller et al.¹⁵ Electrical cardioversion was performed without antiarrhythmic drug pretreatment in the postabsorptive state during light general anesthesia by using 20 mg of etomidate intravenously. Two investigators (I.C.V.G. and A.T.M.G.) managed all procedures at the coronary care unit. A calibrated defibrillator (Hewlett Packard 43120-A, Hewlett-Packard Co, Palo Alto, Calif) that could store 360 J of energy was used as the cardioverter device. One paddle was placed in the second intercostal space on the right side parasternally; the other was placed in a left-sided lateral position along the midaxillary line. According to the protocol, we started with 50 J of stored energy. Thereafter, the energy load of successive shocks was doubled until sinus rhythm was restored or after 2 attempts with 360 J. Postshock rhythm monitoring was secured by using telemetry for 8 to 24 hours. Successful cardioversion was defined as the maintenance of sinus rhythm more than 8 hours after cardioversion. If, after the first electrical cardioversion procedure, sinus rhythm was accomplished, patients did not receive an antiarrhythmic drug. At any rate, 1, 3, and 6 months after discharge, patients were scheduled for outpatient department visits. Thereafter, patients were seen each 6 months. Treatment with anticoagulants was discontinued if sinus rhythm remained present for more than 1 month after its restoration, except in those who required prolonged anticoagulation (eg, in the case of mitral stenosis). If atrial fibrillation relapsed, patients underwent a repeated electrical cardioversion as soon as possible. Those who clearly thought that the recurrence of atrial fibrillation lasted less than 24 hours were subjected to cardioversion without preceded anticoagulation; the others

RESULTS

OUTCOME OF SERIAL CARDIOVERSIONS

Baseline characteristics of the patients are presented in **Table 1**. The mean \pm SD follow-up of the 236 patients was 3.7 ± 1.6 (range, 0.2–7.0) years. **Figure 2** shows the percentage of patients who maintained sinus rhythm after a single cardioversion and after serial cardioversions. The actuarial cumulative percentages of patients who maintained sinus rhythm was 42%, 38%, and 27% after 12, 24, and 48 months, respectively. The steep drop in sinus rhythm maintenance probability at “0” months is an illustration of an unsuccessful cardioversion and an early relapse rate. The gradual decline in time shows the delay of recurrence of atrial fibrillation in the group of patients who were treated with the serial cardioversion approach. Long-term maintenance of sinus rhythm was achieved in 74 patients: 36 were not treated with antiarrhythmic drugs, 7 received sotalolol, 7 received flecainide, and 24 received amiodarone. **Figure 3** shows that half of the successfully treated patients maintained sinus rhythm after only 1 or 2 cardioversions and without prophylactic drug therapy. The number of patients who

took advantage of electrical cardioversion did not increase after the fourth procedure (**Figure 3**). Baseline characteristics of the patients who kept sinus rhythm after serial cardioversions compared with those who did not, including the results of the univariate analysis, are also listed in Table 1. Multivariate analysis revealed that the previous duration of the arrhythmia, New York Heart Association class for exercise tolerance, and age were significantly associated with outcome. Previous arrhythmia duration and age showed a nonlinear distribution of estimated coefficients; therefore, multivariate analysis was done after subdividing the groups as follows: age younger and older than 56 years and duration of the arrhythmia less than 3, 3 to 36, and more than 36 months. The New York Heart Association classification was divided into a group of patients in class I or II and in class III. Multivariate analysis showed that compared with the reference group, patients with a duration of the arrhythmia between 3 and 36 months showed a moderately elevated risk ratio, whereas those with a duration of greater than 36 months had a strongly increased risk ratio of failure of therapy. A moderately elevated risk ratio was also found in patients older than 56 years and in patients in the functional class III (**Table 2**). **Figure 4** shows the

were given warfarin for at least 1 month. Patients with successive recurrences of the arrhythmia were treated consecutively with 3 different prophylactic antiarrhythmic drugs. Until 1989, we used flecainide acetate as the initial agent, but the results of the Cardiac Arrhythmia Suppression Trial¹⁶ turned our preference to sotalol hydrochloride (160-320 mg/d); we used flecainide acetate (200-300 mg/d) as the second agent, and finally, we used amiodarone hydrochloride (600 mg/d for 4 weeks, followed by 200-300 mg/d). Amiodarone therapy was started at 4 or more weeks prior to a repeated electrical cardioversion. Patients with a relapse of atrial fibrillation after more than 1 year of sinus rhythm (ie, a so-called late recurrence) underwent electrical cardioversion without subsequent prophylactic antiarrhythmic drug treatment or without a change of the antiarrhythmic drug that was eventually used. Patients in whom a certain antiarrhythmic drug was contraindicated continued to receive the next agent in our sequence. The inclusion started on the day of the first cardioversion, and follow-up was completed in the case of death or on January 1, 1994, whichever came first.

Conditions for acceptance of atrial fibrillation included failure with amiodarone therapy, drug-related side effects, completely asymptomatic arrhythmia experience after cardioversion(s), or refusal of another electrical cardioversion. In these patients, the ventricular rate control of atrial fibrillation was pursued by digitalis and, if necessary, with additional verapamil hydrochloride, diltiazem hydrochloride, or a β -blocker with the aim to obtain a resting heart rate of less than 100 beats per minute. Bundle of His ablation with implantation of a pacemaker was offered to the patient if symptoms of palpitations were severe or in the case of progression or persistence of tachycardia-related heart failure.

Cardiovascular events included recurrence of atrial

fibrillation, incidence of thromboembolic complications, occurrence of bleeding complications due to the use of anticoagulants, progression of congestive heart failure, and, finally, antiarrhythmic drug-related adverse events. Requirement for pacemaker implantation because of a sick sinus syndrome or bundle of His ablation was also scored. The overall and cardiovascular mortality rates were recorded.

A 2-sided probability level of less than .05 was considered to indicate statistical significance. For the comparison of clinical characteristics associated with long-term maintenance of sinus rhythm and success of cardioversion, a χ^2 test, Wilcoxon-Mann-Whitney *U* test, or Student *t* test, if appropriate, were used. Cumulative rates for the time to recurrence of atrial fibrillation were estimated by using the Kaplan-Meier method. Groups were compared by using the log rank statistic with regard to cumulative rates for the time to an event. To determine parameters that were related to maintenance of sinus rhythm after cardioversion(s), Cox proportional hazards regression analysis was performed. Only covariates with *P* values of .20 or less in the univariate analysis were entered in this model. Variables, modeled as continuous, were assessed by determining the quartiles of their distribution. Subsequently, coefficients for each quartile were determined. In the case of a linear trend of the estimated coefficients of the different groups, the variable was introduced as continuous. If no linearity could be demonstrated, the variable was categorized by taking together the quartiles with similar coefficients. By using the same method, parameters that related to successful cardioversion were determined by using logistic regression analysis. Adjusted risk ratios and 95% confidence intervals (CIs) are presented. For calculations, commercially available computer software (Statistical Analysis System version 6.10, SAS Institute, Cary, NC) was used.

significance of the presence of either 1 or more risk factors compared with the absence of risk factors in relation to outcome. The delay of arrhythmia acceptance was most pronounced in patients without or with only 1 risk factor.

CLINICAL CHARACTERISTICS ASSOCIATED WITH LONG-TERM MAINTENANCE OF SINUS RHYTHM AFTER THE SINGLE CARDIOVERSION PROCEDURE

The first cardioversion was successful in 143 patients (61%). Sinus rhythm was restored after 1 shock (50 J) in only 5 patients, after 2 shocks (50 and 100 J) in 43 patients, after 3 shocks (50, 100, and 200 J) in 47 patients, after 4 shocks (50, 100, 200, and 360 J) in 43 patients, and after 5 shocks (50, 100, 200, and twice 360 J) in 5 patients. In the other 93 patients, sinus rhythm was not restored despite the delivery of twice the highest level of energy. Multivariate analysis revealed that only the previous arrhythmia duration was associated with failure to establish sinus rhythm. Previous atrial fibrillation with a duration of 3 to 36 months and exceeding 36 months was associated with a 4-fold (95% CI, 2-11; *P*=.003) and

a 23-fold (95% CI, 8-66; *P*<.001) increased failure rate, respectively, compared with an arrhythmia existence of less than 3 months. The Kaplan-Meier survival analysis showed that after a single cardioversion without prophylactic antiarrhythmic drug use, 24 patients (10%) maintained long-term sinus rhythm (Figure 2). In the remaining 212 patients, either the first electrical cardioversion was unsuccessful (*n*=93) or there was a relapse of atrial fibrillation (*n*=119). Univariate analysis showed that duration of the arrhythmia, patients' age, and presence of hypertension were significant determinants for a relapse of atrial fibrillation after a single shock and without prophylactic drug treatment. As given in **Table 3**, these parameters retained significance after multivariate analysis.

CARDIOVASCULAR EVENTS

The various cardiovascular events are listed in **Table 4**; these are stratified to the presence of risk factors that are associated with failure of the serial cardioversion strategy. It can be readily deduced that the incidence of events rose sharply in line with the number of arrhythmia risk factors. Congestive heart failure and cardiovascular death

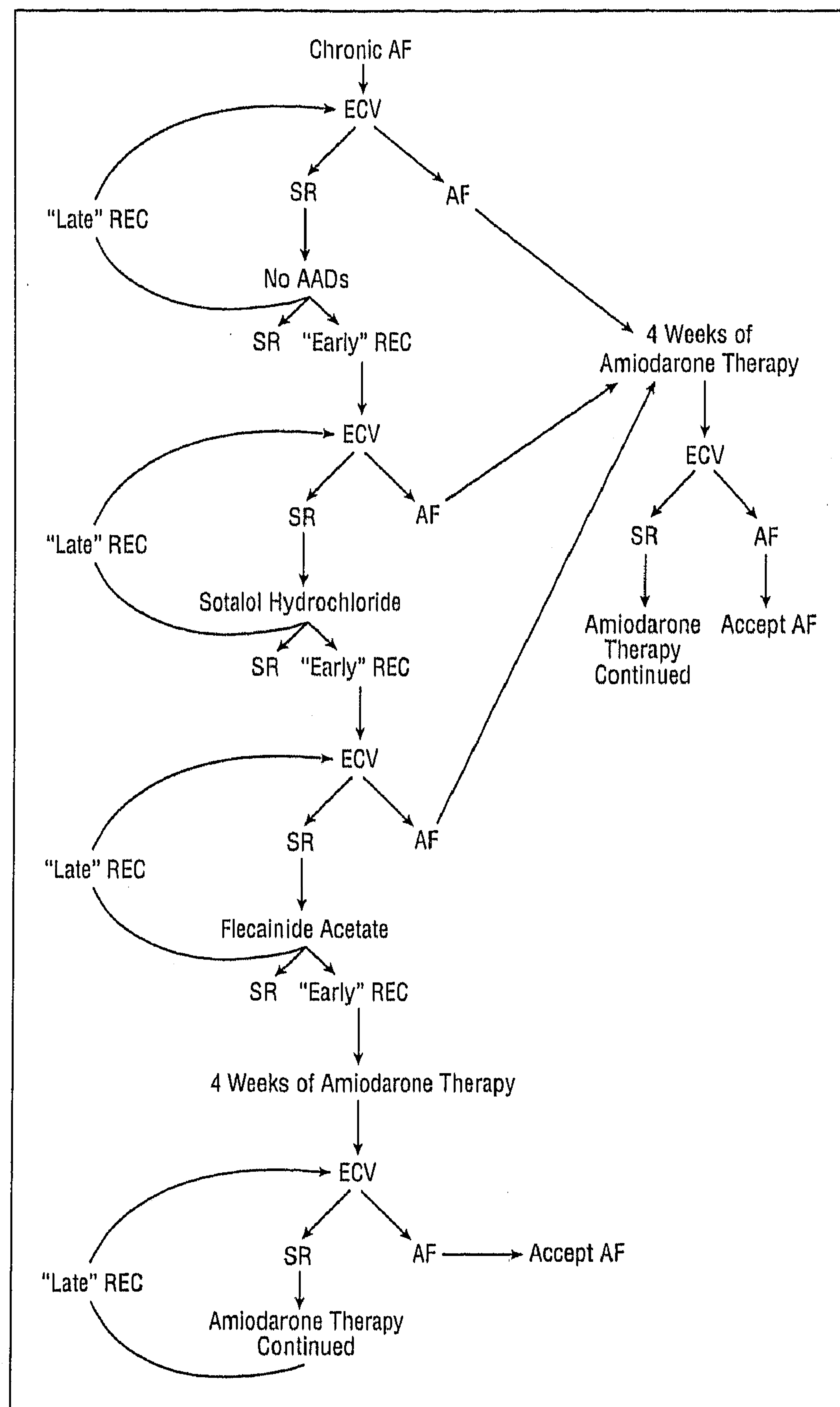


Figure 1. Serial electrical cardioversion protocol. AADs indicates antiarrhythmic drugs; AF, atrial fibrillation; "early" REC, recurrence within 1 year; ECV, electrical cardioversion; "late" REC, recurrence after 1 year; and SR, sinus rhythm.

were the most frequent events. Two patients were admitted to the neurology department because of nonfatal ischemic strokes at 689 and 430 days after restoration of sinus rhythm. At that time, they both showed a recurrence of atrial fibrillation, while they were not being treated with anticoagulants. The first patient was a 60-year-old woman with a history of hypertension who suffered from a hemiparesis. Previous echocardiography showed a normal left ventricular function and a left atrial size within the normal range. She recovered almost completely. The second patient was a 74-year-old man with a history of coronary artery disease who had a hemiparesis. Previously, his left ventricular function was normal, but the left atrium was slightly enlarged. He did not recover from the hemiparesis. Neither of these patients suffered an earlier thromboembolic event. The total incidence of thromboembolic complications per patient-year in our study amounted to 0.2%. A comparison with the findings of other studies is given in **Table 5**. Hemorrhagic complications that led to a hospital admission occurred in 13 patients during total follow-up; all

occurred while they were receiving coumarin and after a mean \pm SD of 302 ± 199 days after inclusion. Two patients suffered a hemorrhagic stroke; in 1 of these patients, it was fatal. Ten patients, of whom 1 died, had bleeding of the gastrointestinal tract. Another patient suffered from a traumatic hemarthrosis. The total incidence of hemorrhagic complications was 1.5 per 100 patient-years; this figure is in good agreement with that of other studies in patients with atrial fibrillation (Table 5). No patient experienced a fall during the study. Overt symptoms of congestive heart failure were frequent during follow-up and occurred predominantly in those patients with preexisting heart failure and other risk factors for atrial fibrillation. Eleven serious adverse events that related to antiarrhythmic drug use were encountered. Each of these events led to withdrawal of the agent: 5 times for amiodarone because of hypothyroidism or skin photoallergy, 3 times for sotalol because of symptomatic hypotension or nightmares, 2 times for flecainide because of progression of congestive heart failure and excessive QRS prolongation, and, finally, once due to digitalis intoxication complicated by paroxysmal atrial tachycardia in a patient with accepted atrial fibrillation. Ventricular proarrhythmia did not occur. Five patients underwent pacemaker implantation: 2 because of sick sinus syndrome and 3 prior to bundle of His ablation. During follow-up, 39 patients (16.5%) died. Mortality was of a cardiovascular origin in 31 patients (13.5%), and 9 of them died suddenly.

COMMENT

In this large-scale prospective study, the efficacy of serial cardioversions in the management of chronic atrial fibrillation was determined during long-term follow-up. Whereas the majority of patients with chronic atrial fibrillation failed to respond to our serial cardioversion strategy, acceptance of the arrhythmia was postponed in many patients who maintained sinus rhythm for some additional years. It is likely that the latter group of patients benefited because they were exposed for a shorter time to the deleterious effects that related to the arrhythmia. We also demonstrated that both the fate of atrial fibrillation and the risk of cardiovascular events are determined by identical factors: duration of the arrhythmia, presence of heart failure, and age. Finally, the present data support the notion that chronic atrial fibrillation treated by serial electrical cardioversion in combination with well-monitored oral anticoagulation is associated with few thromboembolic events.

Like previous studies, we also showed that an increasing duration of atrial fibrillation inversely correlates with the chance of reinstitution of sinus rhythm.²³⁻²⁶ Unexpectedly, however, a duration of atrial fibrillation as short as 3 months impaired the success of the serial cardioversion therapy. Perhaps this already is related to generated permanent morphological changes in the atria at that time, whereas tachycardia-induced changes (eg, electrical remodeling²⁷) are probably more easily reversible. The obvious clinical consequence is that cardioversion should be performed as early as possible after onset of the arrhythmia, preferably within 3 months. In this

Table 1. Baseline Characteristics of Patients With a Successful Serial Cardioversion Approach vs Patients in Whom This Approach Failed

Characteristic	Patients			P*
	Total Group	Success With Serial Cardioversion	Failure With Serial Cardioversion	
No. of patients	236	74	162	...
Mean±SD age, y	63±12	60±13	64±12	.02
Age, y†				
≤56	27	44	24	...
57-63	21	20	21	...
64-70	27	20	28	...
≥71	25	16	27	...
Sex ratio, M/F	133:103	41:33	92:70	.89
Underlying heart disease, % of patients‡				
Coronary artery disease	28	27	28	.79
Rheumatic heart disease	17	11	20	.21
Nonrheumatic valvular heart disease§	16	21	13	.29
Hypertension	17	14	18	.37
Chronic obstructive pulmonary disease	8	8	9	.79
Cardiomyopathy	7	10	6	.36
Congenital heart disease	3	0	4	.03
"Lone" atrial fibrillation	22	26	20	.26
Miscellaneous	3	1	4	.31
Duration of atrial fibrillation, mo¶	9	4	20	.001
<3	25	39	22	...
3-9	26	27	26	...
9-36	23	24	24	...
≥36	26	10	28	...
New York Heart Association, %				
Class I	31	34	30	.02
Class II	45	53	42	...
Class III	24	13	28	...
Mean±SD dimensions, mm				
L atrial size	46±8	44±6	47±8	.02
R atrial size	61±8	59±8	62±8	.01
L ventricular end-diastolic diameter	53±9	52±9	53±9	.67
L ventricular end-systolic diameter	38±10	37±10	38±10	.57

*P value of univariate analysis is shown.

†Data for the age ranges are given as the percentages of patients.

‡More than 1 underlying disease per patient was scored.

§Nonrheumatic valvular heart disease included atherosclerotic mitral regurgitation, 13 patients; mitral regurgitation due to chorda rupture, 1 patient; congenital mitral stenosis plus valve replacement, 1 patient; mitral valve prolapse, 4 patients; aortic regurgitation, 6 patients; and aortic stenosis, 11 patients.

||Miscellaneous included 2 patients after corrected hyperthyroidism, 3 patients with sick sinus syndrome and with an artificial pacemaker, 1 patient after pulmonary surgery, and 1 patient with alcohol abuse.

¶Median values are given; data for the month ranges are given as the percentages of patients.

regard, efficacy of the cardioversion approach will be enhanced by patient counseling, including explanation of the symptoms suggestive for recurrence of the arrhythmia, and if that is the matter, to realize an urgent appointment with their cardiologist.

The low efficacy of the single-shock approach for restoration and maintenance of sinus rhythm is in contrast with previous findings. This may be explained by other investigators' exclusion of patients for whom an initial cardioversion failed. In contrast, our study included patients in whom sinus rhythm could not be restored after a single cardioversion. Second, the duration of follow-up was shorter in other studies compared with that of the present study. Recently, Coplen et al¹¹ summarized 6 quinidine studies and reported that 69%, 58%, and 50% of patients maintained sinus rhythm for 3, 6, and 12 months, respectively. A similar progressive pat-

tern of relapses in the course of follow-up has been reported for disopyramide phosphate, flecainide, propafenone hydrochloride, sotalol, and amiodarone.^{1-8,13,14,23} Thus, the duration of follow-up has often been too short to qualify correctly patients as being "cured," because many will suffer a relapse of the arrhythmia after the follow-up period. From our study, it may also be learned that patients younger than 57 years with a duration of atrial fibrillation of less than 36 months and without hypertension are likely to be cured of chronic atrial fibrillation after only 1 shock and without the start of therapy with an antiarrhythmic drug. Although this group represented only 10% of the present population, costs and risks for these patients can be dramatically reduced by using the electrical cardioversion approach.

The impact of prophylactic antiarrhythmic drugs appears to be limited. Only some patients have responded

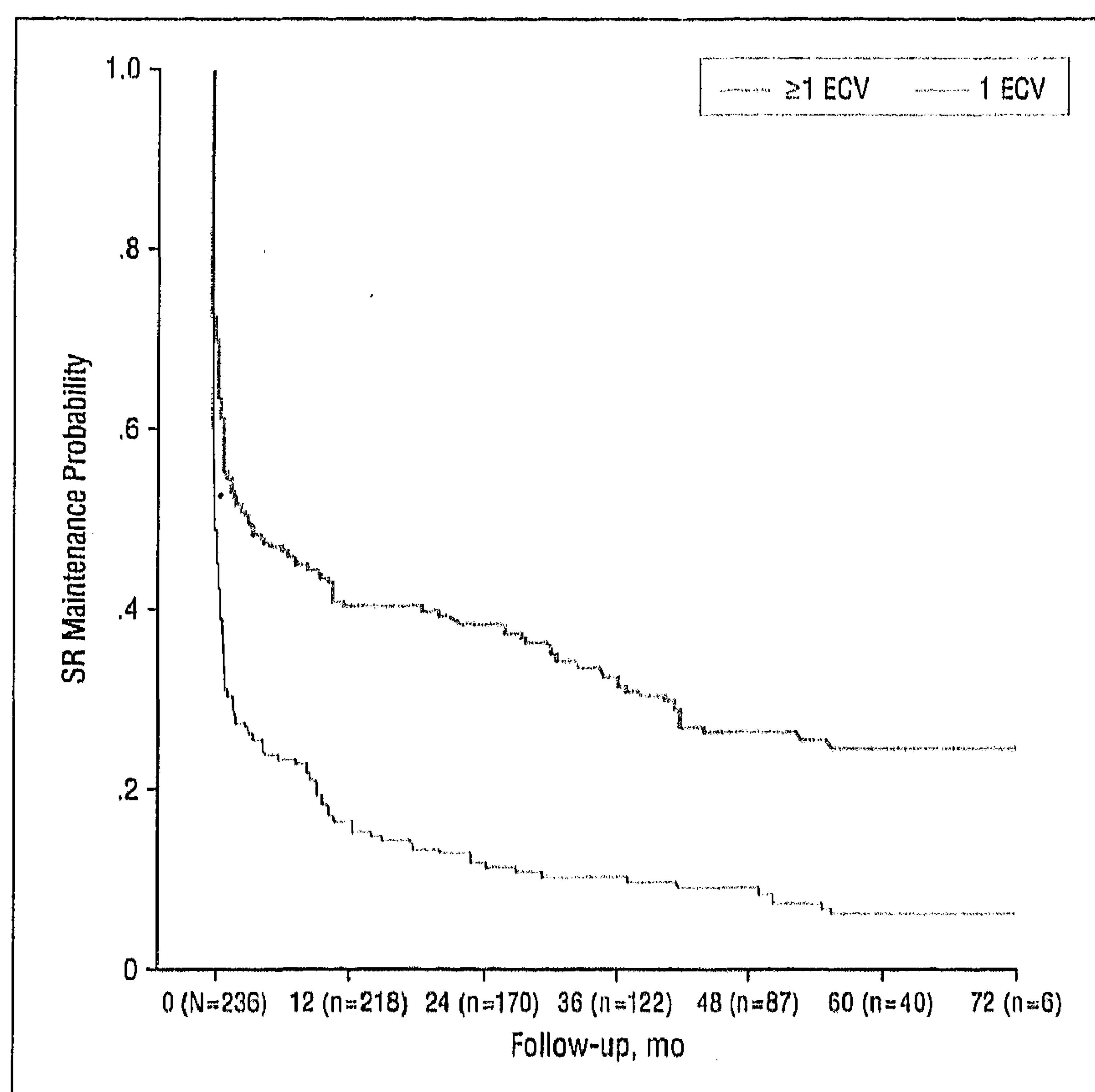


Figure 2. Kaplan-Meier plots depicting the probability of maintenance of sinus rhythm (SR) after serial electrical cardioversions (≥ 1 electrical cardioversion [ECV]) compared with a single cardioversion without drug prescription (1 ECV). N indicates the number of patients at risk during serial cardioversion therapy.

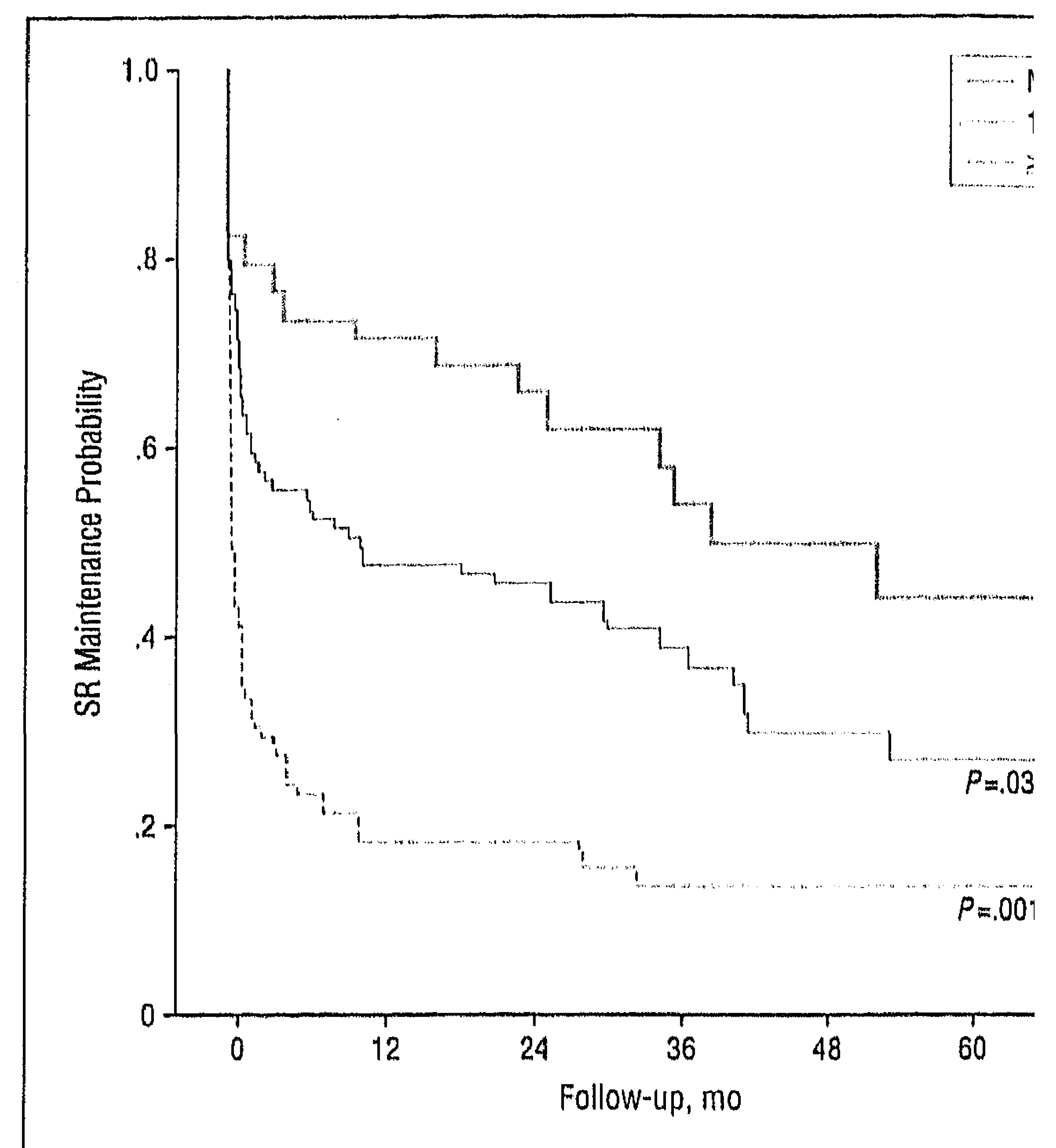


Figure 4. Kaplan-Meier plots depicting the probability of maintenance of sinus rhythm (SR) after serial cardioversions in relation to the presence of risk factors (previous arrhythmia duration >36 months; functional III; and age >56 years). RF indicates risk factor.

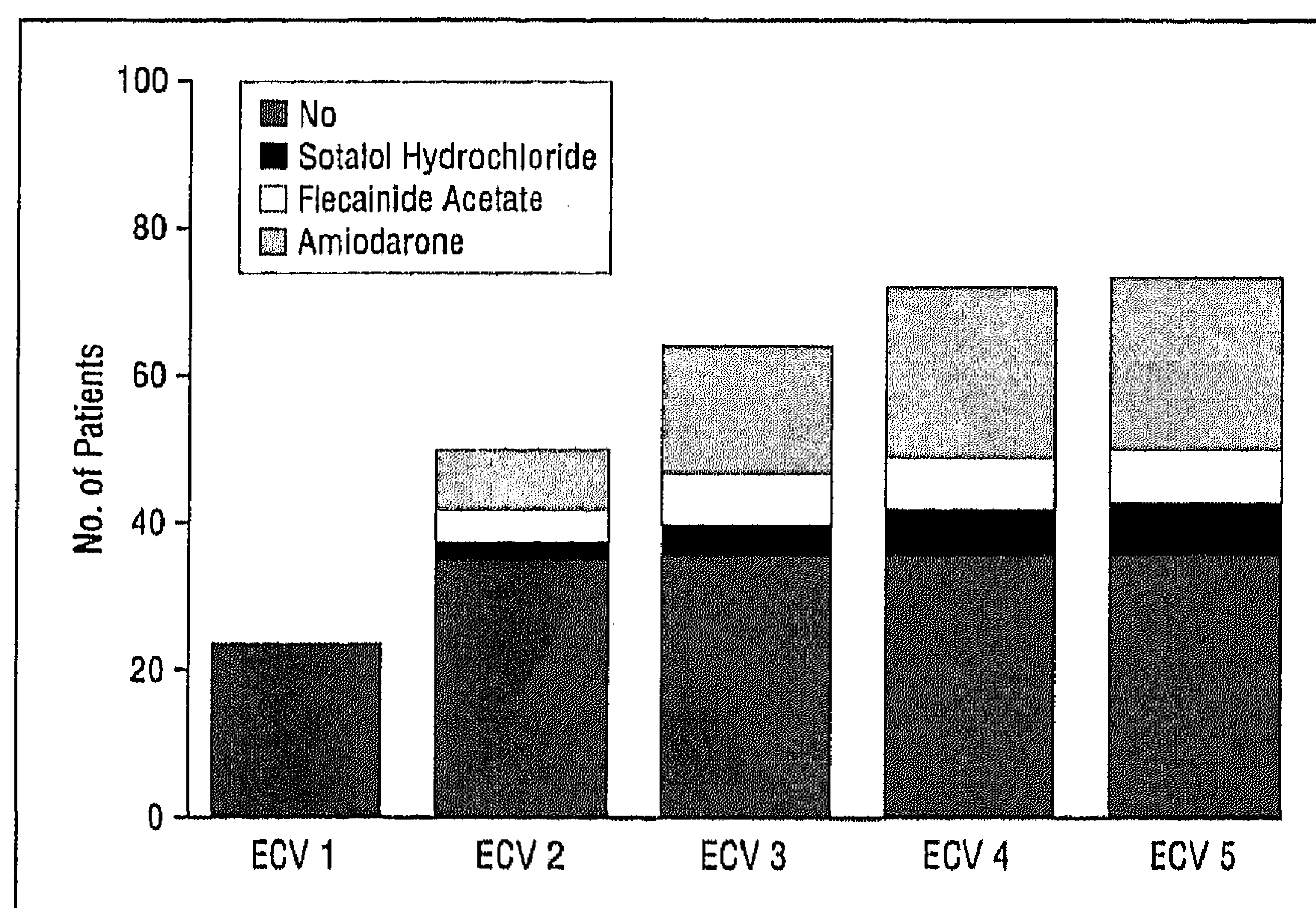


Figure 3. Cumulative number of patients in sinus rhythm classified according to the number of electrical cardioversions (ECV) and type of drug in use at that moment. No indicates no antiarrhythmic drug therapy.

Table 2. Results of Cox Proportional Hazards Regression Analysis: Risk on Failure of Serial Cardioversion Therapy

Risk Factor	Adjusted Risk Ratio	95% Confidence Interval	P
Duration of atrial fibrillation, mo*			
3-35	2.1	1.3-3.4	.002
≥ 36	5.0	3.0-8.3	$<.001$
New York Heart Association class			
III†	1.8	1.3-2.6	.001
Age >56 y‡	1.5	1.0-2.2	.04

*Reference category atrial fibrillation duration less than 3 months with an adjusted risk ratio of 1.0.

†Reference category New York Heart Association classes I and II with an adjusted risk ratio of 1.0.

‡Reference category age of 56 years or younger with an adjusted risk ratio of 1.0.

Table 3. Results of Cox Proportional Hazards Regression Analysis: Risk on Failure of Maintenance of Sinus Rhythm After the Single Cardioversion Procedure

Risk Factor	Adjusted Risk Ratio	95% Confidence Interval
Duration of atrial fibrillation ≥ 36 mo*	2.5	1.8-3.4
Age >56 y†	1.5	1.1-2.1
Hypertension present	1.5	1.1-2.2

*Reference category atrial fibrillation duration less than 36 months with an adjusted risk ratio of 1.0.

†Reference category age of 56 years or younger with an adjusted risk ratio of 1.0.

to therapy with sotalol or flecainide. On the other hand, amiodarone was rather successful; this finding is in agreement with that of earlier reports.^{7,8,23} It is impossible to draw conclusions concerning the prophylactic efficacy of these drugs because the present study was not a randomized one, and there was no control group.

The hypothesis that our serial cardioversion approach, in combination with a relatively high level of anticoagulation, may restrict the incidence of thromboembolic events without increasing the rate of bleeding complications was supported by comparison of our results with those of other trials on the effects of anticoagulation in patients with atrial fibrillation (Table 5). Except for a somewhat younger mean age and characteristics such as the presence of congestive heart failure and left atrial size were about similar in our patients compared with those of the other recent studies. Thus, we believe that our results may not be ascribable to a favorable selection of patients. Currently, the is-

Table 4. Major Cardiovascular Events in Relation to the Presence of the Arrhythmia Risk Factors*

Cardiovascular Event	No. (%) of Patients			
	Total Group (N=236)	No Risk Factor (n=39)	1 Risk Factor (n=108)	≥2 Risk Factors (n=89)
Ischemic thromboembolic complication	2 (1)	0	2 (2)	0
Hemorrhagic complications, including hemorrhagic stroke	13 (5.5), 2 (1)	0, 0	10 (9), 2 (2)	3 (3.5), 0
Congestive heart failure, including valvular surgery	33 (14), 8 (3.5)	3 (7.5), 1 (2.5)	10 (9), 3 (3)	20 (22.5), 4 (4.5)
Adverse events caused by antiarrhythmic drugs	11 (5)	0	8 (7.5)	3 (3.5)
Pacemaker implantation	5 (2.5)	0	3 (3)	2 (2)
Cardiovascular death	31 (13.5)	3 (7.5)	8 (7.5)	20 (22.5)
Total	95 (41.5)	6 (15)	41 (38)	48 (54)

*Risk factors were a duration of atrial fibrillation of 36 months or greater, functional New York Heart Association class III, and age older than 56 years.

Table 5. Incidence of Embolic and Bleeding Complications During the Present Study Compared With That of Previous Studies*

Source, y	No. of Patients	INR	Mean Follow-up, y	Patient-Years	Mean Age, y	Mean L Atrial Size, mm	% of Patients		TECs/ Patient-Years	Bleeding/ Patient-Years†
							Chronic Atrial Fibrillation	Congestive Heart Failure		
Petersen et al, ¹⁷ 1989	335	2.8:4.2	2	413	73	...	100	50	1.2	2.7
SPAF I, ¹⁸ 1991	210	2.0:4.5	1.3	263	65	46	62	14	2.3	1.5
BAATAF, ¹⁹ 1990	212	1.5:2.7	2.3	487	69	42	83	24	0.4	1.6
Connolly et al, ²⁰ 1991	187	2.0:3.0	1.3	237	68	46	94	24	2.5	2.1
Ezekowitz et al, ²¹ 1992	260	1.5:2.7	1.8	489	67	...	100	31	0.9	1.5
SPAF II, ²² 1994										
Age, ≤75 y	358	2.0:4.5	3.1	1110	64	17	1.3	1.7
Age, >75 y	197	2.0:4.5	2.0	394	80	52	3.6	4.2
Present study	236	2.4:4.8	3.7	873	63	46	100	69	0.2	1.5

*Only subgroups that were treated with oral anticoagulants were used for comparison. INR indicates international normalized ratio; TECs, thromboembolic complications; SPAF I, Stroke Prevention in Atrial Fibrillation Study I; BAATAF, Boston Area Anticoagulation Trial for Atrial Fibrillation; and SPAF II, Stroke Prevention in Atrial Fibrillation Study II.

†Bleeding complications that necessitated hospitalization.

unsettled whether a serial electrical cardioversion strategy that is aimed at maintaining sinus rhythm reduces morbidity or mortality in patients with chronic atrial fibrillation. To deal with this problem, a controlled comparison of cardioversion vs rate control treatment has recently been suggested.²⁸ Obviously, that study should compare morbidity and mortality, but it should also compare the costs of treatment and quality of life.

In summary, the present results indicate that young patients (age <57 years) with atrial fibrillation of less than 3 months' duration and a fair exercise tolerance (New York Heart Association functional class I or II) but without hypertension are highly likely to respond to 1 single cardioversion. There is no need to treat these patients with prophylactic antiarrhythmic drugs. On the other hand, electrical cardioversion should be avoided in elderly patients (age >70 years) with a duration of atrial fibrillation that exceeds 36 months and a poor exercise tolerance (New York Heart Association functional class III or IV). Finally, the serial electrical cardioversion approach with the start of therapy with prophylactic antiarrhythmic drugs is worthwhile in patients younger than 71 years who have a duration of atrial fibrillation of less than 36 months and a fair exercise tolerance (New York Heart Association functional class I or II). Improvement of the treat-

ment of the latter group may further be obtained by more frequent patient counseling and explanation of the symptoms associated with a recurrence of the arrhythmia so that they may seek professional care earlier (ie, when the conditions for electrical cardioversion are most optimal).

Accepted for publication July 2, 1996.

Supported by a grant from the Dutch Heart Foundation (Dr Van Gelder).

Presented in part at the 67th Annual Scientific Session of the American Heart Association, Dallas, Tex, November 16, 1994, and at the 16th Annual Scientific Session of the North American Society of Pacing and Electrophysiology, Boston, Mass, May 4, 1995.

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